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LETTER TO THE EDITOR

Male Health

Mixed extragonadal germ cell tumor arising from the prostate: a rare combination

Shu-Guang Liu[1,2], Bin Lei[1,2], Xue-Nong Li[1,2], Xiao-Dong Chen[3], Shuang Wang[1,2], Lin Zheng[1,2], Hai-Li Zhu[1,2], Pei-Xin Lin[1,2], Hong Shen[1,2]

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Dear Editor,

We report a rare case of a mixed germ cell tumor (GCT) that most likely arose from the prostate and included four components: an immature teratoma, a seminoma, an embryonal carcinoma and an endodermal sinus tumor (EST).

A 47-year-old man was admitted to Nanfang Hospital of the Southern Medical University, Guangzhou, China with complaints of dysuria and gross hematuria that had been present for 2 weeks. On admission, rectal palpation revealed a prostate tumor. The serum prostate-specific antigen, beta-human chorionic gonadotropin and carcinoembryonic antigen levels of the patient were within normal limits, but the alpha-fetoprotein (AFP) level was elevated to 509.5 $\mu g l^{-1}$ (the normal range is less than 10.0 $\mu g l^{-1}$). A pelvic positron emission tomography-computed tomography scan revealed a large tumor at the neck of the urinary bladder and the prostate. The mass had an irregular shape and heterogeneous inner tissues. The tumor occupied most of the prostate and exhibited an inhomogeneous density and focal hypermetabolism on a positron emission tomography scan (**Figure 1**). Systemic radiologic examination revealed no evidence of metastatic tumors. A cystoscopic tissue biopsy was performed. The results revealed marked atypia of the tumor cells, which were arranged with a glandular and cribriform architecture. Massive necrosis and hemorrhage were found in the specimen. Therefore, a diagnosis of adenocarcinoma originating from the prostate was made.

The patient underwent radical prostatectomy and pelvic lymphadenectomy via the retropubic approach. The entire prostate gland, seminal vesicles, bladder neck and the pelvic lymph nodes were removed. The mass measured 11 cm × 8 cm × 6 cm. The base of the tumor was located at the neck of the urinary bladder and was connected to the prostate. After the operation, the patient received four courses of BEP chemotherapy that consisted of 30 mg bleomycin on days 1, 8 and 15; 40 mg cisplatin on days 1–4; and 100 mg etoposide on days 1–5. The serum AFP level was reduced to 10.6 $\mu g l^{-1}$ after 5 months of treatment. The patients still complained of difficulty urinating after the procedure. Follow-up data indicated the patient was still alive 16 months after discharge.

[1]Department of Pathology, Nanfang Hospital, [2]Department of Pathology, School of Basic Medical Sciences, Southern Medical University, Guangzhou; [3]Department of Pathology, Guangzhou General Hospital of Guangzhou Military Command, Guangzhou, China.
Correspondence: Dr. H Shen (shenhong2010168@163.com)
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Histologically, massive necrosis was observed in the specimen. The amount of normal prostatic tissue was minimal. Immature teratoma was the predominant component of the specimen and accounted for 60% of the entire tumor, which contained such tissues as epidermal and glandular tissue, immature cartilage, immature striated muscle and primitive neuroepithelium (**Figure 2a–2c**). The second component (accounting for approximately 25%) was seminoma. The tumor cells were arranged in solid nests with a fibrous stromal network, which was characterized by abundant clear cytoplasm, conspicuous membranes, vesicular nuclei and prominent nucleoli. Many lymphocytes had infiltrated the fibrous septae (**Figure 2d**). Based on morphological appearance, embryonal carcinoma composed a small portion of the specimen (approximately 5%) and included gland-like lumina surrounded by pleomorphic cells. These cells were cuboidal with glassy nuclei and ill-defined cellular borders. Cells undergoing mitosis were numerous (**Figure 2e**). EST accounted for approximately 10% of the entire tumor and exhibited adenoidal, reticular or microcystic architectures with fibrous or myxoid stroma. Although the tumor was negative for Schiller–Duval bodies, many hyaline intracellular or extracellular globules were found (**Figure 2f**).

Immunohistochemical study revealed that the seminoma portion of the specimen was positive for C-kit, placental alkaline phosphatase and neuron-specific enolase (**Figure 2g–2i**) and that the Ki67 labeling index (i.e., the number of Ki67-positive cells per 1000 cells as counted at a magnification of 400×) exceeded 60%. The embryonal carcinoma cells stained positively for AE1/AE3 and CD30 (**Figure 2j** and **2k**). AFP-positive staining was found in the EST portion (**Figure 2l**).

Primary extragonadal germ cell tumors are uncommon, and majority of these tumors likely originate from the midline of the body. To date, fewer than 20 cases of primary prostatic malignant GCTs have been described following teratoma, seminoma or EST presentations.[1–3] Only two cases of combined germ cell tumor of the prostate have previously been reported in the English literature.[4,5]

Although the etiology of extragonadal GCTs is not clearly defined, there are two hypotheses about the histogenesis of primary GCT. The first hypothesis suggests that GCTs may originate from pluripotent stem cells that can transform into neoplastic germ cells.[6] For example, EST may occur in the stomach and endometrium. The other hypothesis suggests that germ cells may be sequestered during their migration along the urogenital ridge to the gonadal ridges and that this occurs most commonly along the midline of the body. This theory may explain the origin of the tumor reported here.

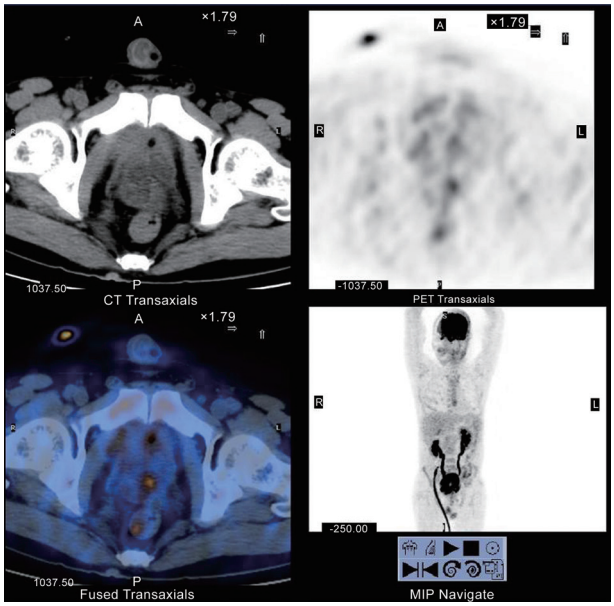

Figure 1: Positron emission tomography-computed tomography showed the tumor occupied most of the prostate and exhibited focal high signal intensity.

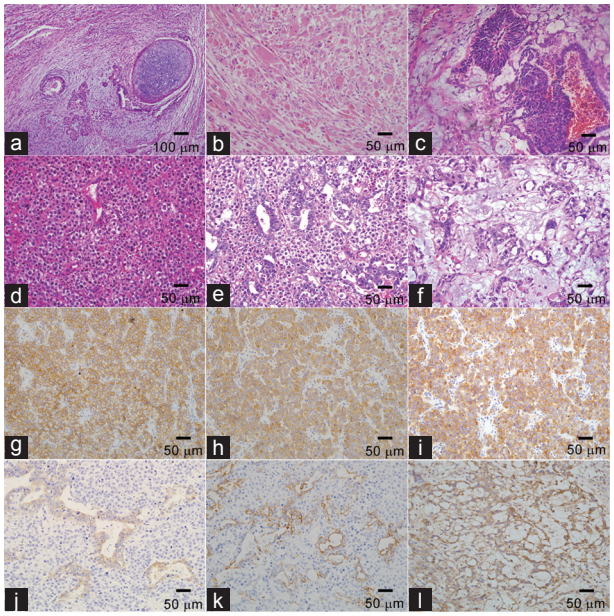

Figure 2: Hematoxylin and eosin (H and E) and immunohistochemical staining of the prostatic tumor. (**a-c**) The components of immature teratoma included epidermal and glandular tissue, immature cartilage, immature striated muscle and primitive neuroepithelium. (**d**) The seminoma cells had abundant clear cytoplasm, conspicuous membranes, vesicular nuclei and prominent nucleoli. Many lymphocytes had infiltrated the fibrous septae. (**e**) Embryonal carcinoma cells arranged gland-like lumina surrounded by pleomorphic cells. These cells were cuboidal with glassy nuclei and ill-defined cellular borders. Mitoses were numerous. (**f**) EST exhibited an adenoidal, reticular or microcystic architecture with fibrous or myxoid stroma. Many hyaline intracellular or extracellular globules were found. (**g–i**) Immunohistochemically, C-kit, placental alkaline phosphatase and neuron-specific enolase staining showed positive reaction on the seminoma portion. (**j, k**) The embryonal carcinoma cells stained positively for AE1/AE3 and CD30. (l) AFP-positive staining was found in the EST portion.

The serum AFP level, the morphological appearance and the immunohistochemical staining for C-kit, placental alkaline phosphatase, AE1/AE3, AFP and CD30 strongly favor the diagnosis of mixed GCT. Although the tumor was predominantly located in the urinary bladder and its growth was limited as it pushed against the prostatic tissue, the urinary bladder is a cystic organ, which allowed sufficient space for the formation of the giant tumor; thus, we hold opinion that this tumor likely originated from the prostate and involved the bladder. The argument that this tumor stemmed from the urinary bladder and not from the prostate could be made; however, both the prostate and bladder neck would have been involved if the tumor originated from the junction between the prostate and bladder. Additionally, a prostate or prostatic parenchyma source of this tumor would be more consistent with literature reports.

Although the prognoses for GCTs are associated with the clinical stage and site of the tumor, the emergence of various components may portend a worse prognosis.[7] However, unlike previous reports, our subject is currently still alive, which we believe may be due to the facts that the focal embryonal carcinoma and the EST in the tumor were small and easy to completely remove in the operation; thus, any residue of the tumor contained only immature teratoma or seminoma components, which were sensitive to chemotherapy and may have regressed or disappeared.

Recognition of the compositions of GCTs is important because the predominant component may determine therapeutic approaches and prognoses. Therefore, this case highlights the importance of awareness about this disease and the role of pathological diagnosis. Further studies are needed to identify the role of chemotherapy in this rare tumor.

AUTHOR CONTRIBUTIONS

SGL and HS collected the data and drafted the manuscript. XNL, XDC and SW carried out the gross examination and final diagnosis. BL and LZ carried out the immunohistochemical study. HLZ and PXL participated in the interpretation of data. All authors have read and approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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